Amendments to the Claims

This listing of claims will replace all prior versions and listings of claims in the application.

1. (currently amended) A composition comprising:

(a) a non-natural molecular scaffold comprising:

(i) a core particle that is a virus-like particle of an RNA bacteriophage ~~selected from the group consisting of:~~

~~(1) a core particle of non-natural origin; and~~

~~(2) a core particle of natural origin~~; and

(ii) an organizer comprising at least one first attachment site, wherein said organizer is connected to said core particle by at least one covalent bond;

(b) an antigen or antigenic determinant with at least one second attachment site,

wherein said antigen or antigenic determinant is amyloid beta peptide ($A\beta_{1-42}$) or a fragment thereof, and wherein said second attachment site is ~~being~~ selected from the group consisting of:

(i) an attachment site not naturally occurring with said antigen or antigenic determinant; and

(ii) an attachment site naturally occurring with said antigen or antigenic determinant,

wherein said second attachment site ~~is capable of association through at least one non-peptide bond to said first attachment site~~ associates with said first attachment site through at least one non-peptide bond; and

wherein said antigen or antigenic determinant and said non-natural molecular scaffold interact through said association to form an ordered and repetitive antigen array.

2. (currently amended) The composition of claim 1, wherein said association is by way of at least one covalent non-peptide bond.

Claims 3-23 (cancelled).

24. (currently amended) The composition of claim 1 [[7]], wherein said virus-like particle of an RNA bacteriophage comprises ~~comprising, or alternatively essentially consisting of,~~ recombinant proteins, or fragments thereof, of ~~a RNA phage~~ an RNA bacteriophage.

25. (currently amended) The composition of claim 1 [[7]], wherein said RNA bacteriophage is ~~virus-like particle comprising, or alternatively essentially consisting of, recombinant proteins, or fragments thereof, of a RNA phage being~~ selected from the group consisting of:

a) bacteriophage Qβ;
b) bacteriophage R17;
c) bacteriophage fr;
d) bacteriophage GA;
e) bacteriophage SP;
f) bacteriophage MS2;
g) bacteriophage M11;
h) bacteriophage MX1;
i) bacteriophage NL95;
k) bacteriophage f2; and
l) bacteriophage PP7.

26. (currently amended) The composition of claim 1 [[7]], wherein said virus-like particle of an RNA bacteriophage comprises ~~comprising, or alternatively essentially consisting of,~~ recombinant proteins, or fragments thereof, of bacteriophage Qβ.

27. (currently amended) The composition of claim 1 [[7]], wherein said virus-like particle of an RNA bacteriophage comprises ~~comprising, or alternatively essentially consisting of,~~ recombinant proteins, or fragments thereof, of bacteriophage fr.

28. (cancelled)

29. (currently amended) The composition of any one of claims ~~7,11,14,18,or~~ 24-27, wherein said second attachment site does not naturally occur with[[in]] said antigen or antigenic determinant.

30. (currently amended) The composition of claim 29, wherein said composition comprises an amino acid linker bound to said antigen or antigenic determinant.

31. (original) The composition of claim 30, wherein said amino acid linker is bound to said antigen or said antigenic determinant ~~by way of~~ through at least one covalent bond.

32. (original) The composition of claim 31, wherein said covalent bond is a peptide bond.

33. (currently amended) The composition of claim 30, wherein said amino acid linker comprises~~, or alternatively consist of,~~ said second attachment site.

34. (original) The composition of claim 33, wherein said amino acid linker comprises a sulfhydryl group or a cysteine residue.

35. (currently amended) The composition of claim 33, wherein said amino acid linker is selected from the group consisting of:

(a) CGG;
(b) an N-terminal gamma 1-linker;
(c) an N-terminal gamma 3-linker;
(d) an Ig hinge region[[s]];
(e) an N-terminal glycine linker[[s]];
(f) $(G)_kC(G)_n$ with n=0-12 and k=0-5;
(g) an N-terminal glycine-serine linker[[s]];
(h) $(G)_kC(G)_m(S)_l(GGGGS)_n$ with n=0-3, k=0-5, m=0-10, l=0-2;
(i) GGC;
(k) GGC-NH2;
(l) a C-terminal gamma 1-linker;
(m) a C-terminal gamma 3-linker;
(n) a C-terminal glycine linker[[s]];

(o) $(G)_nC(G)_k$ with n=0-12 and k=0-5;

(p) a C-terminal glycine-serine linker[[s]]; and

(q) $(G)_m(S)_l(GGGGS)_n(G)_oC(G)_k$ with n=0-3, k=0-5, m=0-10, l=0-2, and o=0-8 (SEQ ID NO: 425).

36. (original) The composition of claim 1, wherein said amyloid beta peptide ($A\beta_{1-42}$) or a fragment thereof is selected from the group consisting of:

(a) Aβ 1-15;

(b) Aβ 1-27;

(c) Aβ 1-40;

(d) Aβ 1-42;

(e) Aβ 33-40; and

(e) Aβ 33-42.

37. (cancelled)

38. (currently amended) The composition of claim 1, wherein said amyloid beta peptide ($A\beta_{1-42}$) or a fragment thereof with said second attachment site has an amino acid sequence selected from the group consisting of:

(a) the amino acid sequence of DAEFRHDSGYEVHHQGGC (SEQ ID NO: 367);

(b) the amino acid sequence of CGHGNKSGLMVGGVVIA (SEQ ID NO: 369); and

(c) the amino acid sequence of DAEFRHDSGYEVHHQKLVF FAEDVGSNGGC (SEQ ID NO: 368).

39. (currently amended) The composition of claim 38, wherein said core particle is ~~selected from the group consisting of:~~

~~a)~~ a virus-like particle comprising~~, alternatively consisting of,~~ recombinant proteins, or fragments thereof, of bacteriophage Qβ; or

~~b)~~ a virus-like particle comprising~~, alternatively consisting of,~~ recombinant proteins, or fragments thereof, of bacteriophage fr~~,~~;

~~c) a virus-like particle of HBcAg-lys-2cys-Mut;~~

~~d)~~ ~~a bacterial pilus; and~~

~~e)~~ ~~a Type 1 pilus of *Escheriehia coli*.~~

40. (currently amended) The composition of claim 36, wherein said first attachment site comprises ~~or is~~ an amino group and said second attachment site comprises ~~or is~~ a sulfhydryl group.

41. (currently amended) The composition of claim 36, wherein said first attachment site comprises ~~or is~~ a lysine residue and said second attachment site comprises ~~or is~~ a cysteine residue.

42. (currently amended) The composition of claim 36, wherein said second attachment site does not naturally occur with[[in]] said antigen or antigenic determinant.

43. (currently amended) The composition of claim 42, wherein said composition comprises an amino acid linker bound to said antigen or antigenic determinant.

44. (currently amended) The composition of claim 43, wherein said amino acid linker is bound to said antigen or said antigenic determinant ~~by way of~~ through at least one covalent bond.

45. (original) The composition of claim 43, wherein said covalent bond is a peptide bond.

46. (currently amended) The composition of 43, wherein said amino acid linker comprises~~, or alternatively consist of,~~ said second attachment site.

47. (original) The composition of claim 46, wherein said amino acid linker comprises a sulfhydryl group or a cysteine residue.

48. (currently amended) The composition of claim 36 or claim 46, wherein said amino acid linker is selected from the group consisting of:

(a) CGG;

(b) an N-terminal gamma 1-linker;

(c) an N-terminal gamma 3-linker;

(d) an Ig hinge region[[s]];

(e) an N-terminal glycine linker[[s]];

(f) $(G)_kC(G)_n$ with n=0-12 and k=0-5;

(g) an N-terminal glycine-serine linker[[s]];

(h) $(G)_kC(G)_m(S)_l(GGGGS)_n$ with n=0-3, k=0-5, m=0-10, l=0-2 (SEQ ID NO: 424);

(i) GGC;

(k) GGC-NH2;

(l) GGC-NHMe;

(m) GGC-N(Me)2;

(n) GGC-NHEt ~~NHET~~;

(o) GGC-N(Et)2;

(p) a C-terminal gamma 1-linker;

(q) a C-terminal gamma 3-linker;

(r) a C-terminal glycine linker[[s]];

(s) $(G)_nC(G)_k$ with n=0-12 and k=0-5;

(t) a C-terminal glycine-serine linkers; and

(u) $(G)_m(S)_l(GGGGS)_n(G)_oC(G)_k$ with n=0-3, k=0-5, m=0-10, l=0-2, and o=0-8 (SEQ ID NO: 425).

49. (currently amended) The composition of claim 36, wherein said amino acid linker is selected from the group consisting of:

(a) CGG;

(b) CGKR (SEQ ID NO: 431);

(c) CGHGNKS (SEQ ID NO: 405);

(d) GGC; and

(e) GGC-NH2[[;]].

50. (currently amended) A pharmaceutical composition comprising:

a) the composition of claim 1; and

b) ~~an acceptable pharmaceutical~~ a pharmaceutically acceptable carrier.

51. (withdrawn – currently amended) A method of ~~immunization~~ immunizing an animal comprising administering the composition of claim 1 to ~~a subject~~ an animal, wherein an immune response against said antigen or antigenic determinant is produced in said animal.

52. (currently amended) A vaccine composition comprising the composition of claim 1 and an adjuvant.

53. (withdrawn – currently amended) A process for producing a non-naturally occurring, ordered and repetitive antigen array comprising:

a) providing a non-natural molecular scaffold comprising:

(i) a core particle that is a virus-like particle of an RNA bacteriophage ~~selected from the group consisting of:~~

~~(1) a core particle of non-natural origin; and~~

~~(2) a core particle of natural origin~~; and

(ii) an organizer comprising at least one first attachment site, wherein said organizer is connected to said core particle by at least one covalent bond; and

b) providing an antigen or antigenic determinant with at least one second attachment site, wherein said antigen or antigenic determinant is amyloid beta peptide ($A\beta_{1-42}$) or a fragment thereof, and wherein said second attachment site ~~being~~ is selected from the group consisting of:

(i) an attachment site not naturally occurring with said antigen or antigenic determinant; and

(ii) an attachment site naturally occurring with said antigen or antigenic determinant~~, wherein said second attachment site is capable of association through at least one non-peptide bond to said first attachment site~~; and

c) combining said non-natural molecular scaffold and said antigen or antigenic determinant[[,]];

wherein said second attachment site associates with said first attachment site through at least one non-peptide bond such that said antigen or antigenic determinant and said non-natural molecular scaffold interact through said association to form an ordered and repetitive antigen array.

54. (new) The composition of claim 1, wherein said organizer is a polypeptide or residue thereof and said second attachment site is a polypeptide or residue thereof.

55. (new) The composition of claim 36, further comprising a heterobifunctional cross-linker.

56. (new) The composition of claim 55, wherein said heterobifunctional cross-linker is selected from the group consisting of:

a) SMPH;

b) Sulfo-MBS; and

c) Sulfo-GMBS.

57. (new) The composition of claim 1, wherein said first attachment site comprises an amino group and said second attachment site comprises a sulfhydryl group.

58. (new) The composition of claim 1, wherein said first attachment site comprises a lysine residue and said second attachment site comprises a cysteine residue.

59. (new) The composition of claim 1, wherein said first attachment site comprises an amino group or a lysine residue.

60. (new) The composition of claim 1, wherein said second attachment site comprises a sulfhydryl group or a cysteine residue.

61. (new) The composition of claim 1, wherein said first attachment site is not a sulfhydryl group.

62. (new) The composition of any one of claims 57-61, wherein said RNA bacteriophage is bacteriophage Qβ.

63. (new) The composition of claim 1, wherein said second attachment site does not naturally occur with said antigen or antigenic determinant.

64. (new) The composition of claim 1, wherein said virus-like particle of an RNA bacteriophage comprises recombinant coat proteins comprising an amino acid sequence selected from the group consisting of:

(a) SEQ ID NO:159;
(b) SEQ ID NO:160;
(c) SEQ ID NO:161;
(d) SEQ ID NO:162;
(e) SEQ ID NO:163;
(f) SEQ ID NO:164;
(g) SEQ ID NO:165;
(h) SEQ ID NO:166;
(i) SEQ ID NO:167;
(j) SEQ ID NO:215;
(k) SEQ ID NO:253;
(l) SEQ ID NO:217; and
(m) SEQ ID NO:254.

65. (new) The composition of claim 1, wherein said virus-like particle of an RNA bacteriophage consists essentially of recombinant coat proteins comprising an amino acid sequence selected from the group consisting of:

(a) SEQ ID NO:159;
(b) SEQ ID NO:160;

(c) SEQ ID NO:161;
(d) SEQ ID NO:162;
(e) SEQ ID NO:163;
(f) SEQ ID NO:164;
(g) SEQ ID NO:165;
(h) SEQ ID NO:166;
(i) SEQ ID NO:167;
(j) SEQ ID NO:215;
(k) SEQ ID NO:253;
(l) SEQ ID NO:217; and
(m) SEQ ID NO:254.

66. (new) The composition of claim 1, wherein said virus-like particle of an RNA bacteriophage comprises recombinant coat proteins having an amino acid sequence of SEQ ID NO:159, or a mixture of coat proteins having amino acid sequences of SEQ ID NO:159 and of SEQ ID NO:217.

67. (new) The composition of claim 1, wherein said virus-like particle of an RNA bacteriophage consists essentially of coat proteins having an amino acid sequence of SEQ ID NO:159, or consists essentially of a mixture of coat proteins having amino acid sequences of SEQ ID NO:217 and of SEQ ID NO:159.

68. (new) The composition of claim 1, wherein said virus-like particle of an RNA bacteriophage comprises one or more coat proteins of said RNA bacteriophage that have been modified by deletion or substitution to remove at least one naturally occurring lysine residue, or that have been modified by insertion or substitution to add at least one lysine residue.

69. (new) The composition of claim 68, wherein said RNA bacteriophage is Qβ.

70. (new) The composition of claim 1, wherein said virus-like particle of an RNA bacteriophage comprises one or more coat proteins comprising an amino acid sequence selected from the group consisting of:

(a) SEQ ID NO:255;
(b) SEQ ID NO:256;
(c) SEQ ID NO:257;
(d) SEQ ID NO:258;
(e) SEQ ID NO:259; and
(f) a mixture of any one of (a)-(e) and the corresponding A1 protein.

71. (new) The composition of claim 1, wherein said virus-like particle of an RNA bacteriophage comprises one or more coat proteins consisting essentially of an amino acid sequence selected from the group consisting of:

(a) SEQ ID NO:255;
(b) SEQ ID NO:256;
(c) SEQ ID NO:257;
(d) SEQ ID NO:258;
(e) SEQ ID NO:259; and
(f) a mixture of any one of (a)-(e) and the corresponding A1 protein.

72. (new) The composition of claim 1, wherein said organizer is an integral part of said RNA bacteriophage.

73. (new) The composition of claim 1, wherein said virus-like particle is a recombinant virus-like particle.

74. (new) A method of treating or preventing Alzheimer's disease comprising administering the composition of claim 1 to an animal, wherein an immune response against said antigen or antigenic determinant is produced in said animal.